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Paternal Effects on the Human Sex Ratio at Birth: Evidence from Interracial Crosses

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SUMMARY

The effects of interracial crossing on the human sex ratio at birth were investigated using United States birth-certificate data for 1972–1979. The sex ratio was 1.059 for approximately 14 million singleton infants born to white couples, 1.033 for 2 million born to black couples, and 1.024 for 64,000 born to American Indian couples. Paternal and maternal race influences on the observed racial differences in sex ratio were analyzed using additional data on approximately 97,000 singleton infants born to white-black couples and 60,000 born to white-Indian couples. After adjustment for mother's race, white fathers had significantly more male offspring than did black fathers (ratio of sex ratios [RSR] = 1.027) and Indian fathers (RSR = 1.022). On the other hand, after adjustment for father's race, white mothers did not have more male offspring than did black mothers (RSR = 0.998) or Indian mothers (RSR = 1.009). The paternal-race effect persisted after adjustment for parental ages, education, birth order, and maternal marital status. The study shows that the observed racial differences in the sex ratio at birth are due to the effects of father's race and not the mother's. The study points to paternal determinants of the human sex ratio at fertilization and/or of the prenatal differential sex survival.

INTRODUCTION

Racial differences in the human sex ratio at birth (secondary sex ratio) have been reported [1]. In the United States, whites have a higher ratio than blacks [2], a finding that has intrigued researchers for decades. Although other factors have

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been reported to affect the sex ratio [3], which can potentially confound the race effect, the white-black difference in sex ratio persists after adjustments have been made for birth order, parental ages, education, and maternal marital status [4, 5], and remains without adequate explanation. Over the past few years, studies have suggested that the secondary sex ratio may depend on the timing of insemination during the menstrual cycle, with more males conceived early and late in the fertile period and more females conceived around the time of ovulation [6, 7]. On the basis of these studies, James recently suggested that the sex ratio may depend on the maternal levels of gonadotropins at the time of fertilization, which could explain the low sex ratio and high twinning rates in blacks [8].

Despite the large number of studies on the human sex ratio, only meager data are available on the effects of interracial crossing on the sex ratio. This approach can potentially sort out paternal from maternal race determinants of the ratio. In a study of the effects of interracial crossing in Hawaii on a variety of perinatal outcomes, no race effects on the secondary sex ratio were found, except for a high ratio among offspring of Korean fathers [9]. This finding, although admittedly based on relatively small numbers, may point to important paternal race influences on the sex ratio. There are, however, no reports in the literature to confirm or refute this finding.

In this study, we investigated the effects of race and interracial crossing on the secondary sex ratio in the United States. We used information on approximately 16.5 million live-born infants derived from birth certificates for 1972–1979. The study focused on the three major race groups in the United States: whites, blacks, and Indians. Racial differences in the secondary sex ratio were found to be due to the effects of father's race.

METHODS

Computerized data derived from live-birth certificates were available to the Centers for Disease Control from the National Center for Health Statistics for the period 1972–1979. The data included 100% of certificates for some states and 50% random samples for the remaining states. For every infant, the data included information on father's and mother's race, obtained either from parents themselves or other informants [10]. In this study, we limited the analysis to singletons who were offspring of the three major parental races (whites, blacks, and American Indians) and their combinations, since fewer babies were born to parents from other race groups and their crosses. We excluded multiple births from this study since twins may have a lower sex ratio than singletons and the incidence of twinning is different in various race groups [11]. We also excluded infants for whom one or both parents had an unspecified race code. These accounted for approximately 10% of live births, mostly with the father's race unknown.

The secondary sex ratios were calculated for offspring of various parental race combinations. To separate paternal and maternal effects on the observed differences in sex ratios for blacks and whites, we analyzed data from black mother-black father couples, white mother-white father couples, black mother-white father couples, and white mother-black father couples. Similar analyses were done for Indian and white couples, but black-Indian couples were not considered because of their small number.

For black and white parents, we calculated the ratio of sex ratios (RSR) for offspring of white-to-black fathers and that of white-to-black mothers. Since parental races were highly correlated, the crude RSRs were adjusted for the other parent's race, using the Mantel-Haenszel procedure [12]. RSRs were further adjusted for six additional demographic

variables coded on birth certificates, using the same procedure. These variables may have independent effects on the sex ratio and included maternal and paternal ages, maternal and paternal education, maternal marital status, and birth order. For these variables, the following stratification groups were used in the Mantel-Haenszel procedure: (1) parental ages (arranged by 5-year intervals), (2) parental education (4 strata: elementary, high-school, college, and unknown), (3) birth order (10 strata: each birth order 1–9+, and unknown), and (4) marital status of mother (3 strata: married, unmarried, and unknown). For Indian and white parents, the same analysis was conducted, and RSRs were calculated for offspring of white-to-Indian fathers and those of white-to-Indian mothers. These were adjusted for the other parent's race as well as for the variables mentioned above.

Last, no adjustment was made in the analysis for the 50% sampling present in some states. This was felt to be justified, since no sex-ratio differences were shown between areas of 50% sampling and those of 100% enumeration.

RESULTS

The numbers of live births on whom birth-certificate data were available between 1972 and 1979 are shown in table 1, grouped by parental race combinations and sex. Offspring of white parents accounted for the vast majority of newborns (86.9%). Offspring of black parents accounted for 11.7% of newborns, but those of Indian parents for only 0.4% of the total. There were 96,956 infants born to white-black parental crosses and 60,385 to white-Indian crosses. Since only 2,729 infants were born to black-Indian parental combinations, these were omitted from further analysis.

The Secondary Sex Ratio by Parental-Race Combinations

(1) *White-Black combinations.* The secondary sex ratio was 1.059 for offspring of white couples and 1.033 for those of black couples (fig. 1). For black and white parents, we calculated the crude ratio of the sex ratios (RSR) for offspring of white-to-black fathers and the ratio for offspring of white-to-black mothers. The crude RSR for white-to-black fathers is 1.025 [(7,436,756/7,022,458)/(1,026,099/993,631), tables 1 and 2] and the ratio for white-to-black mothers is also 1.025 [(7,468,509/7,053,698)/(995,905/964,077), tables 1 and 2]. Among offspring of white-black couples, those born to white fathers had a sex ratio of 1.046 (9,512/9,092, table 1), larger than that of infants born to black fathers (1.027; 39,706/38,646, table 1). The paternal-race effect was confirmed by the statistical analysis shown in table 2. After adjustment for mother's race, white fathers had significantly more male offspring than did black fathers (RSR = 1.027). On the other hand, after adjustment for father's race, white mothers did not have more male offspring than did black mothers (RSR = 0.998). The paternal-race effect persisted (RSR = 1.026) after further adjustments for possible confounding by parental ages, education, birth order, and maternal marital status.

A straightforward adjustment for confounding, such as that just described using the Mantel-Haenszel procedure, is most appropriate if there are no statistical interactions. A search for such interactions was made, and none were found. As an example of this search, table 3 presents a tabulation of the data by parental race and birth order. From among the extraneous variables considered in this study, birth order was chosen for this example since it was the most powerfully related to the sex ratio.

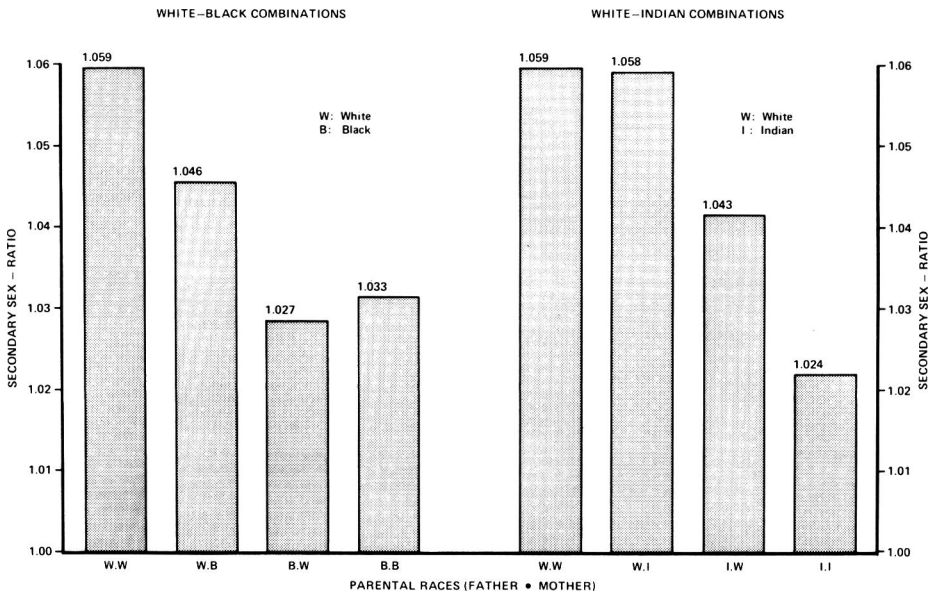

FIG. 1.—Sex ratios by parental-race combinations; U.S. birth-certificate data, 1972–1979

The first step in this search for interaction was to fit these data with a hierarchical linear logistic regression model including the interactions. None of these interactions was found to be significant. Next, a model that included only paternal race, maternal race, and birth order was fitted. The results of this fitting indicate that both paternal race and birth order are independently and significantly related to the sex ratio, whereas maternal race is not. Thus, the analyses confirm the

TABLE 1

NO. LIVE BIRTHS BY SEX AND PARENTAL-RACE GROUPS; U.S. BIRTH-CERTIFICATE DATA, 1972–1979

MOTHER'S RACE		FATHER'S RACE			
		White	Black	Indian	Total
White	M*	7,412,558	39,706	16,245	7,468,509
	F*	6,999,482	38,646	15,570	7,053,698
	T*	14,412,040	78,352	31,815	14,522,207
Black	M	9,512	986,393	319	995,905
	F	9,092	954,985	338	964,077
	T	18,604	1,941,378	657†	1,959,982‡
Indian	M	14,686	1,030	32,391	47,077
	F	13,884	1,042	31,630	45,514
	T	28,570	2,072†	64,021	92,591‡
Total	M	7,436,756	1,026,099	48,636	8,511,491
	F	7,022,458	993,631	47,200	8,063,289
	T	14,459,214	2,019,730‡	95,836‡	16,574,780

* M = male, F = female, T = total.
† Sex-ratio analysis not done because of small nos.
‡ Excludes black-Indian combinations.

TABLE 2

CRUDE AND ADJUSTED RATIOS OF SEX RATIOS (RSRs) FOR OFFSPRING OF WHITE-TO-BLACK AND WHITE-TO-INDIAN PARENTS. ANALYSIS OF PATERNAL- AND MATERNAL-RACE EFFECTS; U.S. BIRTH-CERTIFICATE DATA, 1972–1979

Parental-race combinations	Crude	Adjusted for other parent's race	Further adjusted*
White-black:			
Paternal effect (white/black)	1.025 (χ^2 = 280.5)†	1.027 (χ^2 = 17.5)	1.026 (χ^2 = 16.1)
Maternal effect (white/black)	1.025 (χ^2 = 263.1)	0.998 (χ^2 = 0.08)	0.996 (χ^2 = 0.33)
White-Indian:			
Paternal effect (white/Indian)	1.028 (χ^2 = 17.8)	1.022 (χ^2 = 5.99)	1.020 (χ^2 = 4.72)
Maternal effect (white/Indian)	1.024 (χ^2 = 12.7)	1.009 (χ^2 = 0.92)	1.007 (χ^2 = 0.57)

* Adjusted for other parent's race, maternal and paternal ages, education, birth order, and maternal marital status.

† χ^2 values obtained either from crude analysis or Mantel-Haenszel procedure ($\chi^2_{0.05}$ = 3.84).

results of the straightforward adjustment procedure (i.e., an independent effect of paternal race) and also indicate its appropriateness.

(2) *White-Indian combinations.* The secondary sex ratio was 1.024 for offspring of Indian couples. As in white-black parental combinations, a paternal-race effect could be shown (fig. 1 and table 2). After adjustment for mother's race, white fathers had more male offspring than did Indian fathers (RSR = 1.022), but after adjustment for father's race, white mothers did not have more male offspring than did Indian mothers (RSR = 1.009). The paternal-race effect persisted after adjustment for the additional variables mentioned above (RSR = 1.020).

TABLE 3

SEX RATIOS BY PATERNAL RACE, MATERNAL RACE, AND BIRTH ORDER; U.S. BIRTH-CERTIFICATE DATA, 1972–1979

	PATERNAL RACE · MATERNAL RACE			
BIRTH ORDER	White · White	White · Black	Black · White	Black · Black
1	1.063 (5,847,901)	1.071 (8,066)	1.027 (35,823)	1.040 (654,387)
2 and 3	1.058 (6,867,339)	1.019 (7,867)	1.025 (33,430)	1.032 (896,994)
4+	1.049 (1,407,640)	1.048 (2,154)	1.049 (7,540)	1.021 (339,552)
Unknown	1.071 (289,160)	1.076 (517)	0.996 (1,559)	1.035 (50,445)

NOTE: Total births are in parentheses. Logistic regression *P*-values corresponding to approximate F statistic to remove term from model—paternal race: .0001; maternal race: .9999; birth order: < .0001.

DISCUSSION

These results show that the racial differences in the secondary sex ratio between whites and blacks, and between whites and American Indians, are due to the effects of father's race, independently of the mother's race and the effects of several potential confounding factors: parental ages, education, maternal marital status, and birth order. The finding is somewhat surprising since most previous studies have focused on maternal determinants of the sex ratio, including sociodemographic factors (e.g., maternal age and parity) [1, 3, 4], and menstrual factors (time of insemination) [6, 7]. Although the intermediate sex ratios of 1.046 for offspring of white fathers and black mothers and 1.043 for offspring of Indian fathers and white mothers may suggest a possible maternal effect, this effect, if present, is probably small and clearly overshadowed by a strong paternal effect.

The study has several limitations. The first concerns the effect of parental hybridity on the sex ratio. Traditionally, offspring of white-black and white-Indian couples have been considered, respectively, as blacks and Indians, both socially [13] and on birth certificates [14]. Thus, many of the so-called black and Indian parents may themselves be the offspring of white-black and white-Indian couples, respectively. This hybridity effect was assessed in the Hawaii study [9] but cannot be addressed in this analysis. Our results may be biased if, for example, among white-black couples, black fathers have a different extent of white admixture than do black mothers. Likewise, among white-Indian couples, Indian fathers may have a different extent of white admixture than do Indian mothers.

The second limitation is the heterogeneity of the Indian population. Since all Indian tribes are coded under one category on birth certificates [14], there is no way to examine possible differences in sex ratio among various tribes. However, such an analysis would be limited by the small numbers of infants born to parents from various tribes, and especially of those born to white-Indian crosses.

The third limitation of our study is the possible influence of an unknown paternal-race code on our results. Since many infants for whom the father's race is unknown may be born out of wedlock, it is clear that our adjustment for marital status is limited only to births with specified parental races. Although this problem cannot be evaluated, available data do not suggest a substantial influence of marital status on the sex ratio [4].

The paternal-race effect on the secondary sex ratio found in this study suggests that paternal factors may be affecting either the sex ratio at fertilization (primary sex ratio) or the differential intrauterine survival of the sexes, or both. The paternal-race effect may operate on the primary sex ratio via biologic and non-biologic mechanisms. Biologic factors could involve differences in spermatogenesis between races. A difference in rates of production of X- and Y-carrying sperms has been previously referred to as meiotic drive [13]. Alternatively, there could be differences in X- and Y-carrying sperms that would lead to differential fertilization abilities (gametic selection). These two processes have been suggested as explanations for the high sex ratio observed among offspring of Korean fathers in the Hawaii study [9]. This seems to be an attractive and simple postulate, but

the literature contains virtually no data to support or refute racial differences in spermatogenesis.

Aside from biologic differences operating around the time of fertilization, one may postulate sociological or cultural differences that may affect the primary sex ratio. Examples of such factors include differences in coital habits in different parental-race combinations. The possibility exists that the paternal-race effect operates through the timing of insemination during the mother's menstrual cycle. However, one would have to assume that the father is the predominant determinant of the timing of sexual intercourse, an assumption that needs to be supported.

On the other hand, the paternal-race effect may operate through differential intrauterine sex survival. A theoretical mechanism involves lethal mutations transmitted by the father and differentially affecting sexes prenatally. Y-linked mutations, for example, could decrease male intrauterine survival and may explain the low sex ratio at birth among blacks and Indians. However, the Y chromosome is believed to contain only a small proportion of the genetic material [15], and such mutations have not been documented in humans. On the other hand, X-linked lethal mutations can affect the secondary sex ratio in various ways, depending on whether they are maternally or paternally transmitted and whether they are recessive or dominant. In theory, paternally transmitted dominant X-linked lethal mutations would decrease female prenatal survival and thus increase the secondary sex ratio. Although both X-linked dominant and Y-linked lethal mutations are theoretically plausible, further data are required to document them.

Another possible paternal-race effect on differential prenatal sex survival is via chromosomal anomalies. Such a mechanism is plausible, since chromosomal anomalies may account for more than one-third of spontaneous abortions [16, 17]. Furthermore, it has been estimated that 1%–2% of recognized conceptions are the result of fertilization by a chromosomally abnormal spermatozoon [18]. However, there are virtually no data on racial differences in sperm chromosomal anomalies and on how these differences could affect the primary or secondary sex ratios. A clue to a possible Y-chromosome-mediated paternal effect comes from racial studies on the length of the Y chromosome. Recent data have suggested racial differences in the length of the Y chromosome, with blacks having a higher incidence of longer Y than do Caucasians, owing to the nonfluorescent segment [19]. In addition, limited data have suggested an association between long Y chromosomes and spontaneous abortion [20, 21]. Further studies are needed to investigate whether the length of the Y chromosome is related to distortion in the sex ratio at birth via selective intrauterine demise of males.

Finally, although this study shows that the racial variation in the sex ratio at birth is strongly affected by the father's race and not by the mother's, other factors may also be contributing to racial differences in sex ratio. Moreover, factors affecting the sex ratio within races remain far from being resolved. It is tempting to postulate an important paternal role in the determination of the sex ratio in different race groups, despite previous suggestion of maternally related factors. After all, the Y chromosome is contributed by the father. The suggestion that male differences in sexual physiologic events (differential gametic production or gametic selection) may determine the primary sex ratio and that paternally

mediated mechanisms may lead to differential prenatal loss of one of the sexes are two theoretical postulates that remain virtually unexplored. Recently, there has been a growing concern about the effect of radiation on reproductive outcomes and the sex ratio in particular [22]. In theory, radiation may affect the sex ratio by producing lethal sex-linked mutations and/or chromosomal anomalies [22]. Although atomic bomb survivors have not been shown to have sex-ratio changes among their offspring [23], several studies have suggested a decrease in sex ratio among offspring of uranium miners [24]. Further research is clearly needed to explore father-mediated environmental influences on the human sex ratio between and within different race groups.

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